HCAPLUS

09/917,215 June 17,2002

```
=> d que
L1          10 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("PROSTAGLANDIN EP3 RECEPTOR
               (HUMAN ISOFORM VI)"/CN OR "PROSTAGLANDIN EP3 RECEPTOR (SWINE
               CLONE P6917)"/CN OR "PROSTAGLANDIN EP3 RECEPTOR (SWINE)"/CN OR
               "PROSTAGLANDIN EP3.ALPHA. RECEPTOR (RAT KIDNEY CLONE PREP3)"/CN
                OR "PROSTAGLANDIN EP3.ALPHA. RECEPTOR (RATTUS NORVEGICUS
               CLONE 15/2)"/CN OR "PROSTAGLANDIN EP3A RECEPTOR (OX ADRENAL
               MEDULLA)"/CN OR "PROSTAGLANDIN EP3B RECEPTOR (OX ADRENAL
               MEDULLA)"/CN OR "PROSTAGLANDIN EP3C RECEPTOR (OX ADRENAL
               MEDULLA)"/CN OR "PROSTAGLANDIN EP3D RECEPTOR (OX ADRENAL
               MEDULLA)"/CN OR "PROSTAGLANDIN EP3D RECEPTOR (RATTUS NORVEGICUS
               )"/CN)
L2           4 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("PROSTAGLANDIN EP2 RECEPTOR
               (DOG CLONE B3A)"/CN OR "PROSTAGLANDIN EP2 RECEPTOR (HUMAN
               LUNG)"/CN OR "PROSTAGLANDIN EP2 RECEPTOR (MOUSE CLONE MP412)"/C
               N OR "PROSTAGLANDIN EP2 RECEPTOR (RATTUS NORVEGICUS CLONE
               .LAMBDA.19A1)"/CN OR "PROSTAGLANDIN EP2 RECEPTOR (RATTUS
               NORVEGICUS CLONE SJ26)"/CN)
L3           4 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("PROSTAGLANDIN EP4 RECEPTOR
               (DOG CLONE N8D 356-AMINO ACID C-TERMINAL TRUNCATED FRAGMENT)"/C
               N OR "PROSTAGLANDIN EP4 RECEPTOR (DOG CLONE N8D)"/CN OR
               "PROSTAGLANDIN EP4 RECEPTOR (HUMAN REDUCED)"/CN OR "PROSTAGLAND
               IN EP4 RECEPTOR (RATTUS NORVEGICUS CLONE 3/4)"/CN)
L7         303 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PROSTANOID RECEPTORS (L)
               EP3"+OLD/CT
L8         250 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PROSTANOID RECEPTORS (L)
               EP4"+OLD/CT
L9         289 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PROSTANOID RECEPTORS (L)
               EP2"+OLD/CT
L15       7405 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "DRUG DELIVERY SYSTEMS (L)
               TOPICAL"+OLD/CT
L16        650 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "DRUG DELIVERY SYSTEMS (L)
               GELS, TOPICAL"+OLD/CT
L17        209 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "DRUG DELIVERY SYSTEMS (L)
               EMULSIONS, TOPICAL"+OLD/CT
L18        209 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "DRUG DELIVERY SYSTEMS (L)
               EMULSIONS, TOPICAL"+OLD/CT
L20        266 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "DRUG DELIVERY SYSTEMS (L)
               SOLNS., TOPICAL"+OLD/CT
L22       7405 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L15 OR L16 OR L17 OR L18) OR
               L20
L23          1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((L1 OR L2 OR L3) OR (L7 OR
               L8 OR L9)) AND L22
```

Searched by Paul Schulwitz (703)305-1954

L23 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:456890 HCAPLUS
DN 133:79365
TI Prostaglandin E agonists for treatment of dry eye
IN Klimko, Peter G.
PA Alcon Laboratories, Inc., USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000038690	A2	20000706	WO 1999-US29733	19991214
	WO 2000038690	A3	20001123		

W: AU, BR, CA, JP, MX, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1998-113574P P 19981224
OS MARPAT 133:79365
AB Compns. and methods for the treatment of dry eye and related diseases in mammals utilizing prostaglandin E receptor agonists are disclosed.
IC ICM A61K031-557
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT **Prostanoid receptors**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**EP4**, agonists; prostaglandin E agonists for treatment of dry eye)
IT **Drug delivery systems**
(**topical**; prostaglandin E agonists for treatment of dry eye)

HCAPLUS


```
=> d que
L1          1330 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HAIR PREPARATIONS (L) GROWTH
                 STIMULANTS"/CT
L5            97 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PROSTANOID RECEPTORS (L)
                 EP"+OLD/CT
L6           289 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PROSTANOID RECEPTORS (L)
                 EP2"+OLD/CT
L7           303 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PROSTANOID RECEPTORS (L)
                 EP3"+OLD/CT
L8            16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PROSTANOID RECEPTORS (L)
                 EP3.ALPHA."+OLD/CT
L9            17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PROSTANOID RECEPTORS (L)
                 EP3.BETA."+OLD/CT
L10            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PROSTANOID RECEPTORS (L)
                 EP3.GAMMA."+OLD/CT
L11            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PROSTANOID RECEPTORS (L)
                 EP3C"+OLD/CT
L12            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PROSTANOID RECEPTORS (L)
                 EP3D"+OLD/CT
L13          250 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PROSTANOID RECEPTORS (L)
                 EP4"+OLD/CT
L14          635 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L5 OR L6 OR L7 OR L8 OR L9
                 OR L10 OR L11 OR L12 OR L13)
L15            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 AND L14
```

L15 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:730519 HCAPLUS
DN 135:267274
TI prostaglandin EP4 receptor agonists for controlling hair growth
IN Kumagai, Hiroki; Yamada, Naohiro; Hayashi, Ryoji; Mori, Takeshi; Isogaya, Masafumi
PA Toray Industries, Inc., Japan
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001072268	A1	20011004	WO 2001-JP2756	20010330
	W: AU, CA, CN, JP, KR, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	EP 1186287	A1	20020313	EP 2001-917702	20010330
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	JP 2000-97542	A	20000331		
	WO 2001-JP2756	W	20010330		

OS MARPAT 135:267274
AB Disclosed are agents for controlling hair growth or hair formation while showing little side effect. These agents contain 5,6,7-trinor-4,8-inter-m-phenylene PGI2 derivs. as prostaglandin EP4 receptor agonists. Hair growth-promoting activities of the compds. were tested with rabbits.
IC ICM A61K007-06
ICS A61P017-14
CC 1-12 (Pharmacology)
Section cross-reference(s): 62
IT **Prostanoid receptors**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**EP4**; prostaglandin **EP4** receptor agonists for controlling hair growth)
IT **Hair preparations**
(**growth stimulants**; prostaglandin EP4 receptor agonists for controlling hair growth)
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

MEDLINE


```
=> d que
L17          764 SEA FILE=MEDLINE ABB=ON  PLU=ON  "RECEPTORS, PROSTAGLANDIN
                 E"/CT
L18          813 SEA FILE=MEDLINE ABB=ON  PLU=ON  L17 OR PROSTAGLANDIN(3A)(EP2
                 OR EP3 OR EP 4 OR EP4 OR EP 2 OR EP 3)
L21            2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L18 AND HAIR?


=> d bib ab hitind 1-2

L21  ANSWER 1 OF 2     MEDLINE
AN   2002060591     MEDLINE
DN   21645891   PubMed ID: 11785955
TI   Expression of prostaglandin E(2) receptor subtypes in mouse hair
     follicles.
AU   Torii Eiko; Segi Eri; Sugimoto Yukihiko; Takahashi Kenzo; Kabashima Kenji;
     Ikai Kohichi; Ichikawa Atsushi
CS   Department of Physiological Chemistry, Faculty of Pharmaceutical Sciences,
     Kyoto University, Sakyo-ku, Kyoto, 606-8501, Japan.
SO   BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2002 Jan 18) 290 (2)
     696-700.
     Journal code: 0372516. ISSN: 0006-291X.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200202
ED   Entered STN: 20020125
     Last Updated on STN: 20020212
     Entered Medline: 20020211
AB   We investigated the mRNA distribution of the prostaglandin (PG) E(2)
     receptor subtypes and cyclooxygenases (COXs) in hair follicles
     of the mouse dorsal skin. In the 3-week hair follicles, which
     are in the anagen phase, EP3 and EP4 mRNA were expressed in the dermal
     papilla cells and the outer root sheath cells located in the hair
     bulb region, respectively. In the 8-week hair follicles, which
     are in the telogen phase, the signals for both EP3 and EP4 mRNAs had
     disappeared. To study the hair cycle-dependent expression of
     mRNAs for the EPs and COXs, an area of dorsal hair was depilated
     from 8-week-old mice. On days 8 and 12 after depilation, EP3 and EP4 mRNA
     were reexpressed in the dermal papilla cells and the outer root sheath
     cells, and the induction of COX-2 mRNA was also observed in the outer root
     sheath cells, the upper area of EP4 expression site. These results suggest
     that EP3 and EP4 receptors may involve in the development and regrowth of
     the hair follicles.
CT   Check Tags: Animal; Male; Support, Non-U.S. Gov't
      Enzyme Induction: PH, physiology
        Hair Follicle: CY, cytology
       *Hair Follicle: ME, metabolism
      In Situ Hybridization
      Isoenzymes: BI, biosynthesis
      Isoenzymes: GE, genetics
      Mice
      Mice, Inbred C57BL
      Prostaglandin-Endoperoxide Synthase: BI, biosynthesis
      Prostaglandin-Endoperoxide Synthase: GE, genetics
```

*RNA, Messenger: BI, biosynthesis
***Receptors, Prostaglandin E: BI, biosynthesis**
Receptors, Prostaglandin E: GE, genetics
CN 0 (Isoenzymes); 0 (RNA, Messenger); 0 (Receptors, Prostaglandin E); EC 1.14.99.- (cyclooxygenase 1); EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)

L21 ANSWER 2 OF 2 MEDLINE
AN 2001298131 MEDLINE
DN 21273355 PubMed ID: 11376908
TI Topical bicuculline to the rat spinal cord induces highly localized allodynia that is mediated by spinal prostaglandins.
AU Zhang Z; Hefferan M P; Loomis C W
CS School of Pharmacy and Division of Basic Medical Sciences, Faculty of Medicine, Memorial University of Newfoundland, St. John's, A1B 3V6, Newfoundland, Canada.
SO PAIN, (2001 Jun) 92 (3) 351-61.
Journal code: 7508686. ISSN: 0304-3959.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200108
ED Entered STN: 20010903
Last Updated on STN: 20010903
Entered Medline: 20010830
AB The purpose of this study was to investigate the allodynic effect of bicuculline (BIC) given topically to the dorsal surface of the rat spinal cord, and to determine if spinal prostaglandins (PGs) mediate the allodynic state arising from spinal GABA(A)-receptor blockade. Male Sprague-Dawley rats (325-400 g) were anaesthetized with halothane and maintained with urethane for the continuous monitoring of blood pressure (MAP), heart rate (HR) and cortical electroencephalogram (EEG). A laminectomy was performed to expose the dorsal surface of the spinal cord. Unilateral application of BIC (0.1 microg in 0.1 microl) to the L5 or L6 spinal segment induced a highly localized allodynia (e.g. one or two digits) on the ipsilateral hind paw. Thus, **hair** deflection (brushing the **hair** with a cotton-tipped applicator) in the presence, but not absence of BIC, evoked an increase in MAP and HR, abrupt motor responses (MR; e.g. withdrawal of the hind leg, kicking, and/or scratching) on the affected side, and desynchrony of the EEG. BIC-allodynia was dose-dependent, yielding ED(50)'s (95% CI's) of 45 ng (31-65) for MAP; 68 ng (46-101) for HR and 76 ng (60-97) for MR. Allodynia was sustained for up to 2 h with repeated BIC application without any detectable change in the location or area of peripheral sensitization. Pretreatment with either the EP(1)- receptor antagonist, SC-51322, the cyclooxygenase (COX)-2 selective inhibitor, NS-398, or the NMDA-receptor antagonist, AP-7, inhibited BIC-allodynia in a dose-dependent manner. The results demonstrate: (a) BIC, applied to the dorsal surface of the spinal cord, induces highly localized allodynia; (b) this effect can be sustained with repeated BIC application; (c) it is evoked by NMDA-dependent afferent input; (d) spinal PGs are synthesized by constitutive COX-2 during BIC-allodynia; and (e) spinal PGs contribute to the abnormal processing of tactile input via spinal EP1-receptors.
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
2-Amino-5-phosphonovalerate: AA, analogs & derivatives
2-Amino-5-phosphonovalerate: PD, pharmacology

Administration, Topical
*Bicuculline: PD, pharmacology
Blood Pressure: DE, drug effects
Blood Pressure: PH, physiology
Cyclooxygenase Inhibitors: PD, pharmacology
Dose-Response Relationship, Drug
Electroencephalography: DE, drug effects
Excitatory Amino Acid Antagonists: PD, pharmacology
*GABA Antagonists: PD, pharmacology
Heart Rate: DE, drug effects
Heart Rate: PH, physiology
Motor Neurons: DE, drug effects
Motor Neurons: PH, physiology
Nitrobenzenes: PD, pharmacology
*Pain Measurement: DE, drug effects
Pain Measurement: MT, methods
*Posterior Horn Cells: DE, drug effects
Posterior Horn Cells: PH, physiology
*Prostaglandins: ME, metabolism
Rats
Rats, Sprague-Dawley
Receptors, Prostaglandin E: AI, antagonists & inhibitors
Spinal Cord: DE, drug effects
Spinal Cord: PH, physiology
Sulfonamides: PD, pharmacology
*Touch: DE, drug effects
Touch: PH, physiology

RN 123653-11-2 (NS 398); 485-49-4 (Bicuculline); 76726-92-6 (2-Amino-5-phosphonovalerate); 85797-13-3 (2-amino-7-phosphonoheptanoic acid)

CN 0 (Cyclooxygenase Inhibitors); 0 (Excitatory Amino Acid Antagonists); 0 (GABA Antagonists); 0 (Nitrobenzenes); 0 (Prostaglandins); 0 (Receptors, Prostaglandin E); 0 (Sulfonamides); 0 (prostanoid receptor EP1)